

**Docket No.:** TIBO-0029

**Application No.:** 09/836,477

**Response to Office Action Dated:** May 13, 2004

**PATENT**

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1. (original) A method of determining a phenotype of a biological sample, comprising:
  - a) obtaining a genetic sequence of the biological sample;
  - b) identifying a mutation pattern of the genetic sequence of the biological sample,wherein said mutation pattern comprises at least one mutation that correlates to resistance to at least one therapy;
  - c) searching a relational genotype/phenotype database for at least one database mutation pattern similar to said mutation pattern of the genetic sequence of the biological sample;
  - d) obtaining at least one database phenotype of the at least one database mutation pattern;and
  - e) determining the phenotype of the biological sample from the at least one database phenotype.
2. (original) The method of claim 1, wherein a series of phenotypes is obtained by repeating steps b) through e) for each therapy in a group of therapies.
3. (original) The method of claim 1, wherein said mutation pattern of the genetic sequence of the biological sample is specific to a therapy.
4. (original) The method of claim 1, wherein the biological sample is obtained from at least one of a plasma sample, a blood sample, a saliva sample, mucous sample, and a tissue sample.
5. (original) The method of claim 1, wherein the biological sample comprises at least one of a virus.
6. (original) The method of claim 5, wherein the virus is a retrovirus.
7. (original) The method of claim 6, wherein the retrovirus is Human Immunodeficiency virus (HIV).

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8. (original) The method of claim 1, wherein said at least one mutation is chosen from a frame shift mutation and a generic alteration.
9. (original) The method of claim 1, wherein the genetic sequence is the genetic sequence of a virus.
10. (original) The method of claim 9, wherein the virus is a retrovirus.
11. (original) The method of claim 10, wherein the retrovirus is HIV.
12. (original) The method of claim 11, wherein the genetic sequence is the genetic sequence of HIV.
13. (original) The method of claim 12, wherein the genetic sequence of HIV is chosen from the genetic sequence of the protease region of the HIV genome, the genetic sequence of the reverse transcriptase region of the HIV genome, and the genetic sequence of the protease region and reverse transcriptase region of the HIV genome.
14. (original) The method of claim 1, wherein the biological sample comprises malignant cells.
15. (original) The method of claim 1, wherein the genetic sequence is the genetic sequence of at least one tumor suppressor gene.
16. (original) The method of claim 1, wherein said mutation pattern of the genetic sequence of the biological sample comprises at least two mutations that correlate to resistance to at least one therapy.
17. (original) The method of claim 1, wherein the search of the relational genotype/phenotype database for at least one sample with a similar mutation pattern uses cluster searches.

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18. (original) The method of claim 1, wherein the database mutation pattern comprises at least one mutation found in said mutation pattern of the genetic sequence of the biological sample.
19. (original) The method of claim 1, wherein the database mutation pattern is a mutation pattern in which at least about 50% of the mutations are identical to said mutation pattern of the genetic sequence of the biological sample.
20. (original) The method of claim 19, wherein the database mutation pattern is a mutation pattern in which at least about 80% of the mutations are identical to said mutation pattern of the genetic sequence of the biological sample.
21. (original) The method of claim 20, wherein the database mutation pattern is a mutation pattern in which at least about 90% of the mutations are identical to said mutation pattern of the genetic sequence of the biological sample.
22. (original) The method of claim 21, wherein the mutations of the database mutation pattern are identical to said mutation pattern of the genetic sequence of the biological sample.
23. (original) The method of claim 1, wherein the phenotype of the biological sample is a mean fold-change in resistance, wherein said mean fold change is obtained from all of the database phenotypes obtained in step d).
24. (original) The method of claim 1, wherein the phenotype of the biological sample is expressed as an  $IC_{50}$ .
25. (original) A method of reporting a phenotype for a biological sample, comprising generating a report having the phenotype determined using the method of claim 1.

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26. (original) A report, comprising the phenotype determined using the method of claim 1.
27. (original) A computer readable media, comprising the phenotype determined using the method of claim 1.
28. (withdrawn) A method of determining a phenotype of a biological sample comprising:
- a) obtaining a genetic sequence of the biological sample;
  - b) searching a relational genotype/phenotype database for at least one database genetic sequence similar to said genetic sequence of the biological sample;
  - c) obtaining a database phenotype of the at least one database genetic sequence; and
  - d) determining the phenotype of the biological sample from the database phenotype.
29. (withdrawn) The method of claim 28, wherein the at least one database genetic sequence is at least about 60% identical to the genetic sequence of the biological sample.
30. (withdrawn) The method of claim 29, wherein the at least one database genetic sequence is at least about 70% identical to the genetic sequence of the biological sample.
31. (withdrawn) The method of claim 30, wherein the at least one database genetic sequence is at least about 80% identical to the genetic sequence of the biological sample.
32. (withdrawn) The method of claim 31, wherein the at least one database genetic sequence is at least about 90% identical to the genetic sequence of the biological sample.
33. (withdrawn) A method of assessing effectiveness of a therapy on a patient, comprising
- a) obtaining a genetic sequence of a biological sample from the patient;
  - b) identifying a mutation pattern of the genetic sequence of the biological sample,
- wherein the mutation pattern comprises at least one mutation that correlates to resistance to at least one therapy;

c) searching a relational genotype/phenotype database for at least one database mutation pattern similar to said mutation pattern of the genetic sequence of the biological sample;

d) obtaining at least one database phenotype of the at least one database mutation pattern;

e) determining the phenotype of the biological sample to the therapy from the at least one database phenotype; and

f) determining whether the phenotype of the biological sample is in a therapeutically effect range.

34. (withdrawn) The method of claim 33, wherein a series of phenotypes is obtained by repeating steps b) through e) for each therapy in a group of therapies.

35. (withdrawn) A method of optimizing therapy for a patient, comprising:

a) obtaining a genetic sequence of a biological sample from the patient;

b) identifying a mutation pattern of the genetic sequence of the biological sample, wherein the mutation pattern comprises at least one mutation that correlates to resistance to at least one therapy;

c) searching a relational genotype/phenotype database for at least one database mutation pattern similar to said mutation pattern of the genetic sequence of the biological sample;

d) obtaining at least one database phenotype of the at least one database mutation pattern;

e) determining the phenotype of the biological sample to the therapy from the at least one database phenotype;

f) repeating steps b) through e) for a group of therapies to obtain a series of phenotypes for the biological sample; and

g) selecting an optimal therapy for the patient from the series of phenotypes.

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36. (withdrawn) A method of designing a therapy for a patient, comprising:
- a) obtaining a genetic sequence of a biological sample of the patient;
  - b) identifying a mutation pattern of the genetic sequence of the biological sample, wherein the mutation pattern comprises at least one mutation that correlates to resistance to at least one therapy;
  - c) searching a relational genotype/phenotype database for at least one database mutation pattern similar to said mutation pattern of the genetic sequence of the biological sample;
  - d) obtaining at least one database phenotype of the at least one database mutation pattern;
  - e) determining the phenotype of the biological sample from the at least one database phenotype;
  - f) repeating steps b) through e) for a group of therapies to obtain a series of phenotypes for the biological sample; and
  - g) designing a therapy for the patient from the series of phenotypes.
37. (withdrawn) A business method, comprising a method of determining a phenotype of a biological sample comprising:
- a) receiving from a health care provider a genetic sequence from a biological sample from the patient;
  - b) identifying a mutation pattern of the genetic sequence of the biological sample, wherein said mutation pattern comprises at least one mutation that correlates to resistance to at least one therapy;
  - c) searching a relational genotype/phenotype database for at least one database mutation pattern similar to said mutation pattern of the genetic sequence of the biological sample;
  - d) obtaining at least one database phenotype of the at least one database mutation pattern from the relational genotype/phenotype database;
  - e) determining the at least one phenotype of the biological sample from the at least one database phenotype; and
  - f) providing the health care provider with a phenotype of the biological sample.

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38. (withdrawn) The business method of claim 37 wherein a series of phenotypes is obtained by repeating steps b) through e) for a group of therapies.

39. (original) A computer program for determining a phenotype of a biological sample comprising:

a) receiving a genetic sequence from a biological sample from the patient;

b) identifying a mutation pattern of the genetic sequence of the biological sample, wherein said mutation pattern comprises at least one mutation that correlates to resistance to at least one therapy;

c) searching a relational genotype/phenotype database for at least one database mutation pattern similar to said mutation pattern of the genetic sequence of the biological sample;

d) obtaining at least one database phenotype of the at least one database mutation pattern from the relational genotype/phenotype database;

e) determining the at least one phenotype of the biological sample from the at least one database phenotype; and

f) providing the phenotype of the biological sample.

40. (original) The computer program of claim 39, wherein a series of phenotypes is obtained by repeating steps b) through e) for a group of therapies.

41. (original) The computer program of claim 40, wherein the phenotype of the biological sample is provided in a report.

42. (original) The computer program of claim 40, wherein the report is in a computer readable media.